

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
8 July 2004 (08.07.2004)

PCT

(10) International Publication Number
WO 2004/056823 A1

(51) International Patent Classification⁷: **C07D 471/04**,
A61K 31/437, A61P 29/00, 29/00, 37/00, 25/00

(21) International Application Number:
PCT/EP2003/014867

(22) International Filing Date:
19 December 2003 (19.12.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0230045.7 23 December 2002 (23.12.2002) GB
0230165.3 24 December 2002 (24.12.2002) GB
0307998.5 7 April 2003 (07.04.2003) GB

(71) Applicant (for all designated States except US): **GLAXO GROUP LIMITED** [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).

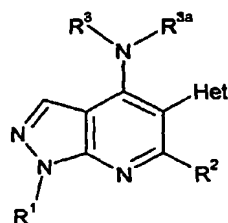
(72) Inventors; and

(75) Inventors/Applicants (for US only): **ALLEN, David, George** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). **COE,**

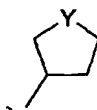
Diane, Mary [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). **COOK, Caroline, Mary** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). **COOPER, Anthony, William, James** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). **DOWLE, Michael, Dennis** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). **EDLIN, Christopher, David** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). **HAMBLIN, Julie, Nicole** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). **JOHNSON, Martin, Redpath** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). **JONES, Paul, Spencer** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). **LINDVALL, Mika, Kristian** [FI/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). **MITCHELL, Charlotte, Jane** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). **REDGRAVE,**

[Continued on next page]

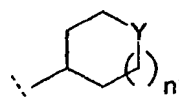
(54) Title: PYRAZOLO[3,4-b]PYRIDINE COMPOUNDS, AND THEIR USE AS PHOSPHODIESTERASE INHIBITORS



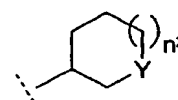
(I)



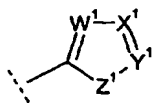
(aa)



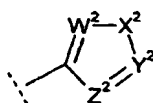
(bb)



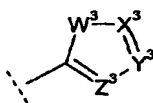
(cc)



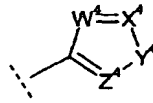
(i)



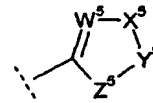
(ii)



(iii)



(iv)



(v)

(57) Abstract: The invention relates to a compound of formula (I) or a salt thereof: Formula (I) wherein: R¹ is C₁₋₄alkyl, C₁₋₃fluoroalkyl or -(CH₂)₂OH; R² is a hydrogen atom (H), methyl or C₁₋₃fluoroalkyl; R^{3a} is a hydrogen atom (H) or C₁₋₃alkyl; R³ is optionally substituted branched C₃₋₆alkyl, optionally substituted C₃₋₈cycloalkyl, optionally substituted mono-unsaturated-C₅₋₇cycloalkenyl, optionally substituted phenyl, or an optionally substituted heterocyclic group of sub-formula (i), or (ii), or (iii), or (iv) or (v). The compounds are phosphodiesterase (PDE) inhibitors, in particular PDE4 inhibitors. Also provided is the use of a compound of formula (I), or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment and/or prophylaxis of an inflammatory and/or allergic disease in a mammal such as a human, for example chronic obstructive pulmonary disease (COPD), asthma, or allergic rhinitis.



Allison, Judith [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB).

(74) Agent: BREEN, Anthony, Paul; GlaxoSmithKline, Corporate Intellectual Property CN925.1, 980 Great West Road, Brentford, Middlesex TW8 9GS (GB).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.